UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,465,458 B1
DATED : October 15, 2002
INVENTOR(S) : Erik H.F. Wong et al.

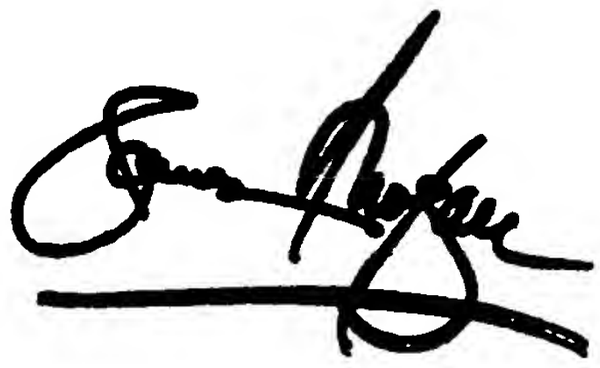
It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 20,
Lines 20-21, should read:

27. The method of claim **26** wherein the oral administration is by a sachet, capsule, tablet,or aerosol spray.

Signed and Sealed this

Eighteenth Day of February, 2003



JAMES E. ROGAN
Director of the United States Patent and Trademark Office

CoFC

(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Letters Patent of:
Erik H.F. Wong et al.

U.S. Patent No. 6,465,458 B1

Issued: October 15, 2002

U.S. Serial No. 09/599,213

Filed: June 22, 2000

Attorney Docket No.: 6248.4

Title: METHOD OF TREATING OR PREVENTING CHRONIC PAIN WITH A HIGHLY SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR

REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 C.F.R. § 1.322

Office of Patent Publication
Commissioner for Patents
Washington, DC 20231

Attn: Certificate of Correction Branch

Dear Sir:

With respect to the above-identified U.S. patent, the patentees and the assignee, through their undersigned attorney, respectfully request expedited issuance of a certificate of correction correcting the patent as noted in the attached "Certificate of Correction" (Form PTO-1050). Attached hereto is a copy of the cover page of the patent and a copy of the last page of the patent, where the error occurs.

Application claim 71 issued as patent claim 27. Patent claim 27 includes a Patent Office typographical error not present in application claim 71. Specifically, patent claim 27 should be corrected to replace "sachet, capsules tablet" with -- sachet, capsule, tablet--. The error in the patent may be verified by reference to the enclosed copy of the "Supplemental Amendment" (Paper 17) originally mailed June 13, 2002, during prosecution of the

application, and to claim 71 therein. Because the typographical error is not attributable to the patentees, assignee, or their attorneys, and the application (as allowed) contained the matter in correct form, no fee is due.

November 13, 2002

Respectfully submitted,

MARSHALL, GERSTEIN & BORUN

By: _____

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Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,465,458 B1

DATED : October 15, 2002

INVENTORS : Erik H.F. Wong et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

~~Claim 27, at~~ column 20, lines 20-21, should read:

27. The method of claim **26** wherein the oral administration is by a sachet, capsule, tablet,or aerosol spray.

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US006465458B1

(12) **United States Patent**
Wong et al.

(10) **Patent No.: US 6,465,458 B1**
(45) **Date of Patent: Oct. 15, 2002**

(54) **METHOD OF TREATING OR PREVENTING CHRONIC PAIN WITH A HIGHLY SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR**

(75) Inventors: **Erik H. F. Wong**, Portage, MI (US); **Saeeduddin Ahmed**, Indinapolis, IN (US); **Robert C. Marshall**, Mattawan, MI (US); **Robert McArthur**, Kalamazoo, MI (US); **Duncan P. Taylor**, Kalamazoo, MI (US); **Lars Birgerson**, Martinsville, NJ (US); **Pasquale Cetera**, Annandale, NJ (US)

(73) Assignee: **Pharmacia & UpJohn Company**, Kalamazoo, MI (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/599,213**

(22) Filed: **Jun. 22, 2000**

Related U.S. Application Data

(60) Provisional application No. 60/170,381, filed on Dec. 13, 1999, provisional application No. 60/158,256, filed on Oct. 6, 1999, provisional application No. 60/144,131, filed on Jul. 16, 1999, and provisional application No. 60/141,968, filed on Jul. 1, 1999.

(51) **Int. Cl.**[7] **A61K 31/535**
(52) **U.S. Cl.** **514/239.2**
(58) **Field of Search** 514/239.2

(56) **References Cited**

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(List continued on next page.)

Primary Examiner—William R. A. Jarvis
(74) *Attorney, Agent, or Firm*—Pharmacia & Upjohn; James D. Damley , Jr.

(57) **ABSTRACT**

Methods and compositions for treating humans suffering from, or preventing a human from suffering, a physiological or psychiatric disease, disorder, or a condition where inhibiting reuptake of norepinephrine is a benefit are disclosed. The methods comprise administering the optically pure (S,S) enantiomer of reboxetine. The methods generally include administration of a therapeutic amount of such compositions. Also disclosed are preparations of a medicament from the composition, and uses of the composition in a manufacture of the medicament to treat a human suffering from, or preventing a human from suffering, a physiological or psychiatric disease, disorder, or condition.

32 Claims, No Drawings

10. The method of claim 9 wherein said composition is orally administered, and further comprising a pharmaceutically acceptable carrier selected from the group consisting of a binder, diluent, lubricant, disintegrating agent, effervescing agent, dyestuff, sweetener, wetting agent, and mixtures thereof.

11. The method of claim 10 wherein the oral administration is by a sachet, capsule, tablet, or aerosol spray.

12. The method of claim 9 wherein said composition is parenterally administered subcutaneously, intraveously, or intramuscularly.

13. The method of claim 1 wherein the pharmaceutically acceptable salt is a methanesulfonate salt.

14. The method of claim 1 wherein the optically pure (S,S) neboxetine or pharmaceutically acceptable salt thereof comprises at least about 90 wt. % of (S,S) roboxetine, and less than about 10 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

15. The method of claim 14 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 97 wt. % of (S,S) reboxetine and less than about 3 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

16. The method of claim 15 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 99 wt. % of (S,S) reboxetine and less than about 1 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

17. A method of treating treating an individual suffering from chronic pain while diminishing adverse side effects, the method comprising the step of administering to the individual a total dose of about 0.1 to about 10 mg/day of an optically pure (S,S) reboxetine, or a pharmaceutically acceptable salt thereof, said optically pure (S,S) reboxetine being substantially free of (R,R) reboxetine.

18. The method of claim 17 wherein said adverse side effects comprise dizziness, insomnia, lightheadedness, changes in blood pressure, sweating, gastrointestinal disturbances, sexual dysfunction in males, anticholinergic-like effects, and side effects with drug-drug interactions.

19. The method of claim 17 wherein said composition is administered in an amount of about 0.5 to about 8 mg/day.

20. The method of claim 19 wherein said composition is administered in an amount of about 0.5 to about 5 mg/day.

21. The method of claim 20 wherein said composition is administered in an amount of about 0.5 to about 2.5 mg/day.

22. The method of claim 21 wherein said composition is administered in an amount of about 0.5 to about 0.9 mg/day.

23. The method of claim 22 wherein said composition is administered in an amount of about 0.5 to about 0.8 mg/day.

24. The method of claim 23 wherein said composition is administered in an amount of about 0.5 to about 0.75 mg/day.

25. The method of claim 17 wherein said composition is administered orally, topically, parenterally, transdermally, rectally, or vaginally.

26. The method of claim 25 wherein said composition is orally administered, and further comprising a pharmaceutically acceptable carrier selected from the group consisting of a binder, diluent, lubricant, disintegrating agent, effervescing agent, dyestuff, sweetener, wetting agent, and mixtures thereof.

27. The method of claim 26 wherein the oral administration is by a sachet, capsules tablet, or aerosol spray.

28. The method of claim 25 wherein said composition is parenterally administered subcutaneously, intraveously, or intramuscularly.

29. The method of claim 17 wherein the pharmaceutically acceptable salt is a methanesulfonate salt.

30. The method of claim 17 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 90 wt. % of (S,S) reboxetine, and less than about 10 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

31. The method of claim 30 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 97 wt. % of (S,S) reboxetine and less than about 3 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

32. The method of claim 31 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 99 wt. % of (S,S) reboxetine and less than about 1 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

* * * * *

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Erik H.F. Wong et al.

Serial No.: 09/599,213

Filed: June 22, 2000

Title: HIGHLY SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITORS AND METHODS OF USING THE SAME

Group Art Unit: 1614

Examiner: William R.A. Jarvis

Attorney Docket No.: 6248.4

I hereby certify that this correspondence is being facsimile transmitted to Examiner William R.A. Jarvis (Group Art Unit 1614) at the U.S. Patent and Trademark Office, facsimile no. (703) 746-3168, on **June 13, 2002**.

Sandip H. Patel (Reg. No. 43,848)
Attorney for Applicants

SUPPLEMENTAL AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend the above-identified application as follows.

In The Claims:

Claim 1 has been amended and is as follows:

1. (Twice Amended) A method of treating an individual suffering from chronic pain, the method comprising the step of administering to the individual a therapeutically effective amount of a composition comprising an optically pure (S,S) reboxetine, or a pharmaceutically acceptable salt thereof, said compound being substantially free of (R,R) reboxetine.

Claim 13 has been canceled, without prejudice.

Claims 14 and 15 have been amended and are as follows:

14. (Amended) The method of claim 1 wherein the pharmaceutically acceptable salt is a methanesulfonate salt.

15. (Amended) The method of claim 1 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 90 wt.% of (S,S) reboxetine, and less than about 10 wt.% of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

Claims 32-38 have been canceled, without prejudice.

New claims 63-76 have been added and are as follows:

63. The method of claim 39 wherein said composition is administered in an amount of about 0.5 to about 8 mg/day.

64. The method of claim 63 wherein said composition is administered in an amount of about 0.5 to about 5 mg/day.

65. The method of claim 64 wherein said composition is administered in an amount of about 0.5 to about 2.5 mg/day.

66. The method of claim 65 wherein said composition is administered in an amount of about 0.5 to about 0.9 mg/day.

67. The method of claim 66 wherein said composition is administered in an amount of about 0.5 to about 0.8 mg/day.

68. The method of claim 67 wherein said composition is administered in an amount of about 0.5 to about 0.75 mg/day.

69. The method of claim 39 wherein said composition is administered orally, topically, parenterally, transdermally, rectally, or vaginally.

70. The method of claim 69 wherein said composition is orally administered, and further comprising a pharmaceutically acceptable carrier selected from the group consisting of a binder, diluent, lubricant, disintegrating agent, effervescing agent, dyestuff, sweetener, wetting agent, and mixtures thereof.

71. The method of claim 70 wherein the oral administration is by a sachet, capsule, tablet, or aerosol spray.

72. The method of claim 69 wherein said composition is parenterally administered subcutaneously, intraveously, or intramuscularly.

73. The method of claim 39 wherein the pharmaceutically acceptable salt is a methanesulfonate salt.

74. The method of claim 39 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 90 wt. % of (S,S) reboxetine, and less than about 10 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

75. The method of claim 74 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 97 wt. % of (S,S) reboxetine and less than about 3 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

76. The method of claim 75 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 99 wt. % of (S,S) reboxetine and less than about 1 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

REMARKS

This paper is being submitted pursuant to a telephonic interview with Examiner Jarvis on June 12, 2002. During the interview, the examiner indicated that the amended and new claims presented herein would be allowable.

Claim 1 has been amended to incorporate the features recited claim 13. Claims 14 and 15 have been amended to now depend from amended claim 1.

Claims 13 and 32-38 have been canceled, without prejudice to filing a continuing application directed to the subject matter of these claims.

Claims 63-76 have been added and are either directly or indirectly dependent upon claim 39. Claims 63-76 mirror originally-filed, dependent claims 3-12 and 14-17.

No new matter has been introduced by this paper.

It is believed that no fees are due for the entry of the 14 new claims in view of payments previously submitted in connection with 14 originally-filed claims that were later withdrawn from consideration (and later canceled) pursuant to a restriction requirement dated August 21, 2001, an official action dated October 10, 2001, and an "Amendment 'A'" submitted March 25, 2002. Any deficiencies, however, or any additional required fee may be charged to our Deposit Account No. 13-2855.

Pursuant to 37 C.F.R. § 1.121, attached hereto are sheets (numbered as pages 6-8) showing the changes made to the claims by this amendment, the first sheet of which is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

CONCLUSION

In summary, the applicants respectfully request: (**a**) cancellation of claims 13 and 32-38; (**b**) entry of the amendments to claims 1, 14, and 15; (**c**) entry of new claims 63-76; and, (**d**) allowance of all claims pending after entry of the foregoing amendments (i.e., claims 1-12, 14-17, 39, 40, and 63-76).

Should the examiner wish to discuss the foregoing, or any matter of form or procedure in an effort to advance this application to allowance, he is urged to contact the undersigned attorney.

Respectfully submitted,

MARSHALL, GERSTEIN & BORUN

June 13, 2002

By: 

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In The Claims:

Please amend claim 1 as follows:

1. (Twice Amended) A method of treating an individual suffering from chronic pain, the method comprising the step of administering to the individual a therapeutically effective amount of a composition comprising [a compound having a pharmacological selectivity of serotonin (K_i)/norepinephrine (K_i) of at least about 5000] an optically pure (S,S) reboxetine, or a pharmaceutically acceptable salt thereof, said compound being substantially free of (R,R) reboxetine.

Please cancel claim 13, without prejudice.

Please amend claims 14 and 15 as follows:

14. (Amended) The method of claim [13] 1 wherein the pharmaceutically acceptable salt is a methanesulfonate salt.

15. (Amended) The method of claim [13] 1 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 90 wt.% of (S,S) reboxetine, and less than about 10 wt.% of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

Please cancel claims 32-38, without prejudice.

Please add new claims 63-76 as follows:

63. The method of claim 39 wherein said composition is administered in an amount of about 0.5 to about 8 mg/day.

64. The method of claim 63 wherein said composition is administered in an amount of about 0.5 to about 5 mg/day.

65. The method of claim 64 wherein said composition is administered in an amount of about 0.5 to about 2.5 mg/day.

66. The method of claim 65 wherein said composition is administered in an amount of about 0.5 to about 0.9 mg/day.

67. The method of claim 66 wherein said composition is administered in an amount of about 0.5 to about 0.8 mg/day.

68. The method of claim 67 wherein said composition is administered in an amount of about 0.5 to about 0.75 mg/day.

69. The method of claim 39 wherein said composition is administered orally, topically, parenterally, transdermally, rectally, or vaginally.

70. The method of claim 69 wherein said composition is orally administered, and further comprising a pharmaceutically acceptable carrier selected from the group consisting of a binder, diluent, lubricant, disintegrating agent, effervescing agent, dyestuff, sweetener, wetting agent, and mixtures thereof.

71. The method of claim 70 wherein the oral administration is by a sachet, capsule, tablet, or aerosol spray.

72. The method of claim 69 wherein said composition is parenterally administered subcutaneously, intraveously, or intramuscularly.

73. The method of claim 39 wherein the pharmaceutically acceptable salt is a methanesulfonate salt.

74. The method of claim 39 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 90 wt. % of (S,S) reboxetine, and less than about 10 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

75. The method of claim 74 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 97 wt. % of (S,S) reboxetine and less than about 3 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.

76. The method of claim 75 wherein the optically pure (S,S) reboxetine or pharmaceutically acceptable salt thereof comprises at least about 99 wt. % of (S,S) reboxetine and less than about 1 wt. % of (R,R) reboxetine, based on the total weight of the (S,S) and (R,R) reboxetine present.